REMARKS

Claims 1-31, 34 and 36-65 are pending in the application. Claims 1-26, 34, 37 and 41-65 are withdrawn. Claims 27-31, 36 and 38-40 are under examination and stand rejected. Claim 27 is amended herein. Support for the claim amendments is provided by the specification at, for example, paragraphs [0009], [0020] and [0066]. No new matter is added by way of these amendments. Applicants respectfully request entry of the claim amendments and reconsideration based on the following remarks.

Objections to the Specification

The Examiner has maintained the objections to the specification. Specifically, the Examiner alleges that various terms in paragraphs [0063] and [0065] are indefinite or are contrary to the definitions set forth in paragraph [0052]. Applicants respectfully traverse.

As explained in the prior response, amendments to the specification requested by the Examiner could be construed as introducing new matter. The Examiner has provided no statutory basis to require such amendments, nor has the Examiner explained how the alleged informalities have any bearing on the claims under examination. Applicants note that none of the terms objected to by the Examiner appear in any of the claims under examination.

Accordingly, Applicants respectfully request that the objections to the specification be withdrawn.

Rejections under 35 U.S.C. § 112, second paragraph

Claims 27-31, 36 and 38-40 are rejected under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite. The Office asserts that essential steps are omitted in claim 27, amounting to a gap between steps. MPEP § 2172.01. Specifically, the Examiner states that the preamble recites a method of "guiding" decisions, while step c) recites the step of "basing" decisions and that whether or how the step of "basing" amounts to "guiding" is not clear. Further, the Office asserts that input parameters and logic structures for "basing" and "guiding" are unclear, and that the

preamble language "said auto antibody production" lacks antecedent basis. Applicants traverse the rejection.

With respect to the phrase "guiding decisions" in the preamble of the claim, applicants respectfully submit that the preamble language is not a limitation of the claimed invention. "If the body of a claim fully and intrinsically sets forth all of the limitations of the claimed invention, and the preamble merely states, for example, the purpose or intended use of the invention, rather than any distinct definition of any of the claimed invention's limitations, then the preamble is not considered a limitation and is of no significance to claim construction." *Pitney Bowes, Inc. v. Hewlett-Packard Co.*, 182 F.3d 1298, 1305, 51 USPQ2d 1161, 1165 (Fed. Cir. 1999). See MPEP § 2111.02(II).

With respect to step c), applicants respectfully submit that a person of skill in the art, for example, a health care provider such as a clinician or nurse, would understand what is meant by the phrase "basing therapeutic decisions" as used herein. Nevertheless, solely to facilitate prosecution, claim 27 is amended to clarify that the therapeutic decision to initiate, terminate, or adjust the level of therapeutic administration of a natural subject is based on the presence of an assessed auto antibody in step b). Support for the claim language is provided by the specification at, for example, paragraphs [0009], [0020] and [0066]. As described in the specification, therapeutic decisions are possible based on the determination that a specific therapeutic inactivating component, such as an auto antibody, is present. *See* specification at, e.g., paragraph [0066]. For example, the specification discloses that the level or concentration of a therapeutic agent administered may be altered based on the presence of such a therapeutic inactivating component. *See* specification at, e.g., paragraph [0066].

Claim 27 is further amended to address the antecedent basis issue raised by the Examiner.

Applicants respectfully submit that the claims, as amended, are clear and definite. Accordingly, applicants respectfully request that the rejection under 35 U.S.C. § 112, second paragraph, be withdrawn.

Rejections under 35 U.S.C. § 102(e)

Claims 27, 28, 30, 31, 36, 39 and 40 are rejected under 35 U.S.C. § 102(e) as allegedly being anticipated by Conti-Fine (U.S. 6,759,385). Applicants traverse the rejection.

In order to show anticipation under 35 USC § 102, the cited reference must teach each and every element of the claimed invention. "A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987). *See* MPEP § 2131. Moreover, the elements must be arranged as required by the claim. However, this is not an *ipsissimis verbis* test, i.e., identity of terminology is not required. *In re Bond*, 910 F.2d 831, 15 USPQ2d 1566 (Fed. Cir. 1990). *See* MPEP § 2131.

The Examiner asserts that Conti-Fine "describes a method [of] guiding therapeutic decisions for a subject afflicted with an antibody specific for a natural substance, wherein said antibody resulted from therapeutic administration of the natural substance." *See* Office action at page 9. Applicants respectfully submit that the Office has isolated short passages of the reference and interpreted them out of context, and thus has not properly appreciated what the reference discloses.

Conti-Fine provides a *therapeutic* method to treat antibody-mediated diseases by administering an "epitope" peptide comprising an epitope sequence derived from a particular antigen (e.g., an exogenously administered protein) associated with the antibody-mediated disease. *See* Conti-Fine at col. 2, lines 9-13. The method is effective to specifically tolerize, or down-regulate, the immune response to the antigen, and significantly, the "epitope" peptide does not include the entire sequence of the antigen. *See* Conti-Fine at col. 2, lines 13-18. Thus, the "epitope" peptide is not a "natural substance" within the scope of claim 27.

The portions of Conti-Fine cited by the Examiner simply do not teach a method of basing therapeutic decisions to initiate, terminate or adjust the level of therapeutic administration of

a natural substance based on the presence of an assessed auto antibody to said natural substance, as claimed.

For example, col. 6, lines 61-62 recites "a method to inhibit or suppress an antibody mediated disease that is associated with the administration of an endogenous protein..." This statement is merely a broad generalization of the therapeutic method described in the reference. As explained on col. 7, lines 15-18, the Conti-Fine method comprises administering a peptide (i.e., the "epitope" peptide) in an amount effective to suppress or tolerize the immune response to the administered endogenous protein. It is unclear to the applicants how the cited portion of Conti-Fine can reasonably be interpreted as "a method of guiding therapeutic decisions."

The Office further cites col. 24 lines, 12-15, which states "the animal is contacted with a particular peptide, or a plurality of peptides, preferably ones which were identified as having immunodominant epitope sequences." This passage refers to administration of an "epitope" peptide to an animal in a method to determine the tolerogenic efficacy of such peptides.

Conti-Fine does not disclose "assessing said sample for the presence of said auto antibody"

The Examiner cites Conti-Fine at col. 24, lines 21-23 as allegedly anticipating steps a) and b), which require a) obtaining a sample from a subject; and b) assessing said sample for the presence of an auto antibody specific for a natural substance, wherein the auto antibody is produced as a result of therapeutic administration of said natural substance.

Specifically, the Examiner has selectively quoted the following passage to support this assertion: "*[T]he amount of antibody specific for the antigen obtained at time periods before immunization and after immunization compared.*" Conti-Fine, col. 24, lines 21-23.

The cited passage of Conti-Fine does not relate to any method of treating a disease or to a method of guiding therapeutic decisions. Rather, it is part of the description of a method to

identify an "epitope" peptide useful for the therapeutic method described by Conti-Fine. In its entirety, the relevant paragraph states:

> Epitope peptides falling within the scope of the invention may also be identified by in vivo assays, such as animal models for a particular indication or disease. Generally, the animal is contacted with a particular peptide, or a plurality of peptides, preferably ones which were identified as having immunodominant epitope sequences. The animal is then immunized with an antigen having sequences corresponding to at least a portion, i.e., the immunodominant epitope sequence, of the peptide. The tolerogenic efficacy of the peptide is then determined. For example, T cells may be isolated from these animals and their response to antigen or peptide in vitro measured, or *the amount of antibody specific for the antigen obtained at time periods before immunization and after immunization compared.* *See* col. 24, lines 10-23.

Read in context, the cited portion of Conti-Fine relates to: (a) administering an "epitope" peptide to an animal (col. 24, lines 12-15); (b) immunizing the animal with an antigen (col. 24, lines 15-17); and (c) determining the tolerogenic efficacy of the epitope peptide (col. 24, lines 18-19) by comparing the amount of antibody specific for the antigen obtained before and after the immunization step (col. 24, lines 21-23). This method, which requires pre-administration of an "epitope" peptide prior to administration of the antigenic substance, and is intended to determine the tolerogenic efficacy of the peptide, is clearly distinguishable from steps a) and b) as claimed. It does not relate to a therapeutic step at all, only to a way of identifying a suitable "epitope" peptide.

Conti-Fine does not disclose "basing therapeutic decisions to initiate, terminate, or adjust the level of therapeutic administration of said natural substance"

The Examiner has cited Conti-Fine at col. 7, lines 43-48 and col. 38, lines 40-45 as allegedly teaching step c), which recites "basing therapeutic decisions to initiate, terminate, or adjust the level of therapeutic administration of said natural substance to said subject based on the presence of said auto antibody in step b)."

Applicants respectfully submit that the Examiner has misread the cited portion of Conti-Fine. Taking appropriate account of the punctuation, col. 7, lines 41-48 of Conti-Fine teaches nasally administering to a mammal "an amount of an epitope peptide, a variant thereof or a combination thereof effective to suppress an immune response to the exogenously introduced protein" (col. 7, lines 45-48) wherein the mammal has "an indication or disease characterized by a decreased amount or a lack of an endogenous protein, [and] wherein the mammal is subjected to exogenous introduction of the protein or the corresponding recombinant polypeptide..." (col. 7, lines 41-45).

As discussed previously, this is a therapeutic method comprising administration of an "epitope" peptide to suppress an immune response to an exogenously administered endogenous protein, in a mammal having a condition characterized by a lack of said endogenous protein. As noted above, the "epitope" peptide does not comprise the full length antigen, i.e., the exogenously administered protein, and thus does not constitute a "natural substance" within the scope of claim 27.

Accordingly, Conti-Fine does not teach step c) of the claimed method, which recites "basing therapeutic decisions to initiate, terminate, or adjust the level of therapeutic administration of said natural substance" to a subject based on the presence of an auto antibody specific for said natural substance in step b).

The Office has failed to establish a *prima facie* case of anticipation

As discussed in detail above, Conti-Fine fails to teach each and every element of claimed methods, and thus does not anticipate the invention as claimed. The seemingly randomly selected passages cited by the Office neither disclose the claim elements nor comply with the requirement that the elements be arranged as required by the claims. Accordingly, the applicants respectfully request that the rejection under 35 U.S.C. § 102(e) be withdrawn.

Rejections under 35 U.S.C. § 103(a)

Claims 29 and 38 are rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Conti-Fine (U.S. 6,759,385) in view of Bunn (346 N. ENGL. J. MED. 522 (2002). Applicants traverse the rejection.

As discussed in detail above, Conti-Fine neither teaches nor suggests the invention as claimed, and this deficiency is not solved by combination with Bunn. Even assuming, *arguendo*, that one of skill in the art would be motivated by Bunn to develop a method to guide therapeutic decisions to initiate, terminate or adjust the level of administration of erythropoietin, Conti-Fine fails to provide such a method for guiding therapeutic decisions. Thus, based on the combination of Conti-Fine and Bunn, a person of skill in the art would not have had a reasonable expectation of success of achieving the invention as claimed.

Accordingly, the Office has failed to establish a *prima facie* case of obviousness. Applicants respectfully request that the rejection under 35 U.S.C. § 103(a) be withdrawn.

CONCLUSION

In view of the above, each of the presently pending claims in this application is believed to be in immediate condition for allowance. Accordingly, the Examiner is respectfully requested to withdraw the outstanding rejection of the claims and to pass this application to issue. If it is determined that a telephone conference would expedite the prosecution of this application, the Examiner is invited to telephone the undersigned at the number given below.

In the event the U.S. Patent and Trademark office determines that an extension and/or other relief is required, applicant petitions for any required relief including extensions of time and authorizes the Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to Deposit Account No. 03-1952 referencing docket no. **532212002000**. However, the Commissioner is not authorized to charge the cost of the issue fee to the Deposit Account.

Dated: July 27, 2007

Respectfully submitted,

By: /Leslie A. Robinson/
Leslie A. Robinson
Registration No.: 54,403
MORRISON & FOERSTER LLP
12531 High Bluff Drive, Suite 100
San Diego, California 92130-2040
(858) 720-5117